

### Listing of the Claims

This listing of claims will replace all prior versions of claims in the application:

1. (currently amended) A penetrating ~~peptide~~module comprising a penetrating peptide and an effector that is coupled or fused to said penetrating peptide, said penetrating peptide comprising at least one amino acid sequence selected from the group consisting of:

- a) ~~(BX)<sub>4</sub>Z(BX)<sub>2</sub>ZXB~~SEQ ID NOS: 1-15;
- b) ~~ZBXB<sub>2</sub>XBXB<sub>2</sub>XBX<sub>3</sub>BXB<sub>2</sub>X<sub>2</sub>B<sub>2</sub>~~SEQ ID NOS: 24-29 and;
- e) ~~————ZBZX<sub>2</sub>B<sub>4</sub>XB<sub>3</sub>ZXB<sub>4</sub>Z<sub>2</sub>B<sub>2</sub>;~~
- d) ~~————ZB<sub>9</sub>XBX<sub>2</sub>B<sub>2</sub>ZBXZBX<sub>2</sub>;~~
- e) ~~————BZB<sub>8</sub>XB<sub>9</sub>X<sub>2</sub>ZXB;~~
- f) ~~————B<sub>2</sub>ZXZB<sub>5</sub>XB<sub>2</sub>XB<sub>2</sub>X<sub>2</sub>BZXB<sub>2</sub>;~~
- g) ~~————XB<sub>9</sub>XBXB<sub>6</sub>X<sub>3</sub>B;~~
- h) ~~————X<sub>2</sub>B<sub>3</sub>XB<sub>4</sub>ZBXB<sub>4</sub>XB<sub>n</sub>XB;~~
- i) ~~————XB<sub>2</sub>XZBXZB<sub>2</sub>ZBX<sub>3</sub>BZBX<sub>3</sub>B;~~
- j) ~~————BZXBXXZ<sub>2</sub>B<sub>4</sub>XBX<sub>2</sub>B<sub>2</sub>XB<sub>4</sub>X<sub>2</sub>;~~
- k) ~~————BZXBXXZ<sub>2</sub>B<sub>4</sub>XBX<sub>2</sub>B<sub>2</sub>XB<sub>4</sub>;~~
- l) ~~————B<sub>2</sub>XZ<sub>2</sub>XB<sub>4</sub>XBX<sub>2</sub>B<sub>5</sub>X<sub>2</sub>B<sub>2</sub>;~~
- m) ~~————B<sub>q</sub>X<sub>1</sub>ZB<sub>m</sub>X<sub>q</sub>B<sub>4</sub>XBX<sub>n</sub>B<sub>m</sub>ZB<sub>2</sub>X<sub>2</sub>B<sub>2</sub>;~~
- n) ~~————B<sub>2</sub>ZX<sub>3</sub>ZB<sub>m</sub>X<sub>q</sub>B<sub>4</sub>XBX<sub>n</sub>B<sub>m</sub>ZB<sub>2</sub>X<sub>2</sub>B<sub>2</sub>;~~
- e) ~~————X<sub>3</sub>ZB<sub>6</sub>XBX<sub>3</sub>BZB<sub>2</sub>X<sub>2</sub>B<sub>2</sub>;~~ and

p<sub>c</sub>) at least 12 contiguous amino acids of any of peptides in a) through or e<sub>b</sub>),

wherein

- q is 0 or 1;
- m is 1 or 2;
- n is 2 or 3;
- t is 1 or 2 or 3; and
- X is any amino acid;
- B is a hydrophobic amino acid; and
- Z is a charged amino acid;

wherein said penetrating peptide is capable of translocating across a biological barrier.

2-9. (canceled)

10. (currently amended) The penetrating ~~peptide~~ module of claim 1, wherein the penetrating peptide comprises amino acid sequence is SEQ ID NO: 24 or at least 12 contiguous amino acids ~~thereof~~ SEQ ID NO:24.

11. (currently amended) The penetrating ~~peptide~~ module of claim 1, wherein the penetrating peptide is less than 30 amino acids long.

12. (currently amended) The penetrating ~~peptide~~ module of claim 1, wherein the penetrating peptide is less than 25 amino acids long.

13. (currently amended) The penetrating ~~peptide~~ module of claim 1, wherein the penetrating peptide is less than 20 amino acids long.

14. (canceled)

15. (currently amended) The penetrating ~~peptide~~ module of claim ~~141~~, wherein said effector is a bioactive peptide.

16. (currently amended) The penetrating ~~peptide~~ module of claim 15, wherein said bioactive peptide is selected from the group consisting of: insulin, growth hormone, a gonadotropin, a growth factor, erythropoietin, granulocyte/monocyte colony stimulating factor (GM-CSF),  $\alpha$ MSH, enkephalin, dalargin, kyotorphin, EPO, bFGF, hirulog, a lutenizing hormone releasing hormone (LHRH) analog, and neurotrophic factors.

17. (currently amended) The penetrating ~~peptide~~ module of claim ~~141~~, wherein said effector is a pharmaceutically active agent.

18. (currently amended) The penetrating ~~peptide~~ module of claim 17, wherein said pharmaceutically active agent is selected from the group consisting of: an anticoagulant, a toxin, an antibiotic, an antipathogenic agent, an antigen, an antibody fragment, an

immunomodulator, a vitamin, an enzyme, an antineoplastic agent, heparin, methotrexate and a therapeutic agent.

19. (currently amended) A method of translocating a the penetrating peptide module of claim 1 across a biological barrier, ~~wherein the penetrating peptide is the penetrating peptide of claim 2~~ the method comprising introducing the penetrating module to a biological barrier.

20. (currently amended) A method of translocating a the penetrating peptide module of claim 10 across a biological barrier, ~~wherein the penetrating peptide is the penetrating peptide of claim 6~~ the method comprising introducing the penetrating module to a biological barrier.

21-25. (canceled)

26. (currently amended) The penetrating ~~peptide module as in any one of claim[[s]] 1, 14,~~ and 25, wherein translocation across a biological barrier occurs within a tissue selected from the group consisting of: epithelial cells and endothelial cells.

27. (currently amended) The penetrating ~~peptide module as in any one of claim[[s]] 1, 14,~~ and 25, wherein said biological barrier is selected from the group consisting of: tight junctions and the plasma membrane.

28-30. (canceled)

31. (currently amended) A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the penetrating ~~peptide module according to~~ claim 25, and a pharmaceutically acceptable carrier.

32. (original) The pharmaceutical composition of claim 31, wherein the composition further comprises a mixture of at least two substances selected from the group consisting of a non-ionic detergent, an ionic detergent, a protease inhibitor; and a reducing agent.

33. (original) The pharmaceutical composition of claim 32, wherein the non-ionic

detergent is a poloxamer.

34. (currently amended) The pharmaceutical composition of claim 33, wherein the poloxamer is pluronic<sup>®</sup> F-68.

35. (original) The pharmaceutical composition of claim 32, wherein the ionic detergent is a bile salt.

36. (currently amended) The pharmaceutical composition of claim 35, wherein the bile salt is ~~Taurodeoxycholate~~ Taurodeoxycholate.

37. (currently amended) The pharmaceutical composition of claim 32, wherein the protease inhibitor is selected from the group consisting of ~~aprotinin~~ aprotinin and soy[[a]] bean trypsin inhibitor.

38. (currently amended) The pharmaceutical composition of claim 32, wherein the reducing agent is N-Acetyl-L-cysteine (NAC).

39. (currently amended) A method of producing ~~a penetrating peptide comprising~~ the penetrating peptide module of claim 1 ~~and an effector~~, said method comprising coupling said effector to said penetrating peptide.

40. (currently amended) The method of claim 39, wherein the coupling of said effector to said penetrating peptide is achieved by a covalent bond.

41. (original) The method of claim 40, wherein said covalent bond is a peptide bond.

42. (original) The method of claim 40, wherein the covalent bond is achieved by a homo- or a hetero-functional bridging reagent.

43. (original) The method of claim 42, wherein the bridging reagent is a succinimidyl-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC)-type reagent.

44. (original) The method of claim 40, wherein the covalent bond is achieved by a peptide linker.

45. (original) The method of claim 44, wherein the peptide linker has the sequence of SEQ ID NO: 16 or SEQ ID NO:17.

46. (original) The method of claim 44, wherein the peptide linker can be cleaved by an enzyme.

47. (currently amended) The method of claim 46, wherein the peptide linker is designed to be cleaved by an enzyme conditionally activated under a certain physiological state and wherein the released effector favorably influences ~~that~~ said physiological state.

48. (currently amended) The method of claim 39, wherein the coupling of said effector to said penetrating peptide is achieved by a non-covalent bond.

49. (currently amended) The method of claim 48, wherein the non-covalent bond is achieved by an attachment of a hydrophobic moiety to the penetrating peptide, wherein the hydrophobic moiety enables the penetrating module peptide to be incorporated at the interface of a hydrophobic vesicle in which the effector is contained.

50. (original) The method of claim 48, wherein the non-covalent bond is the result of a biotin-avidin or biotin-streptavidin interaction.

51-52. (canceled)

53. (original) A kit comprising, in one or more containers, a therapeutically or prophylactically effective amount of the pharmaceutical composition of claim 31.

54. (original) A method of treating or preventing a disease or pathological condition, said method comprising administering to a subject in which such treatment or prevention is desired,

the pharmaceutical composition of claim 31, in an amount sufficient to treat or prevent said disease or said pathological condition in said subject.

55. (original) The method of claim 54, wherein said disease or said pathological condition is selected from a group consisting of endocrine disorders, diabetes, infertility, hormone deficiencies, osteoporosis, neurodegenerative disorders, Alzheimer's disease, Parkinson's disease, Huntington's disease, cardiovascular disorders, atherosclerosis, hypercoagulable states, hypocoagulable states, coronary disease, cerebrovascular events, metabolic disorders, obesity, vitamin deficiencies, haematological disorders, and neoplastic disease.

56. (currently amended) A method for producing the penetrating ~~peptide~~ module of claim 25 1 comprising

- a) transfecting a production cell with a vector comprising a nucleic acid molecule of a fusion protein encoding said penetrating peptide and an effector operably linked to an expression control sequence;
- b) culturing said production cell under conditions that permit production of a fusion protein consisting of the penetrating peptide and an effector peptide; and
- c) isolating said fusion protein.

57-62. (canceled)

63. (currently amended) ~~A peptide comprising an amino acid sequence~~ The penetrating module of claim 1, wherein said penetrating peptide is derived from a human neurokinin receptor, and ~~said peptide~~ is characterized by the ability to penetrate biological barriers *in vivo*.

64-67. (canceled)

68. (currently amended) The penetrating module of claim ~~64~~ 1, ~~wherein the further comprising a~~ molecular vessel is selected from the group consisting of a soluble receptor, a minireceptor, and a binding protein, wherein said penetrating peptide is coupled or fused to the molecular vessel, which encloses the effector.

69. (original) The penetrating module of claim 68, wherein the soluble receptor is a soluble insulin receptor.

70. (original) The penetrating module of claim 69, wherein the effector is insulin.

71. (original) The penetrating module of claim 68, wherein the minireceptor is the ligand-binding domain of the insulin receptor.

72. (original) The penetrating module of claim 71, wherein the effector is insulin.

73. (original) The penetrating module of claim 68, wherein the binding protein is Intrinsic factor.

74. (original) The penetrating module of claim 73, wherein the effector is vitamin B12.

75. (currently amended) A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the penetrating module according to claim [[64]]68, and a pharmaceutically acceptable carrier.

76. (currently amended) A method for producing the penetrating peptide module of claim 25 1 comprising using solid-phase peptide synthesis of the peptide.

77. (currently amended) The penetrating peptide module of claim 15, wherein the bioactive peptide further comprising comprises a chemical modification.

78. (currently amended) The penetrating peptide module of claim 77, wherein said bioactive peptide is selected from the group consisting of: insulin, growth hormone, a gonadotropin, a growth factor, erythropoietin, granulocyte/monocyte colony stimulating factor (GM-CSF),  $\alpha$ MSH, enkephalin, dalargin, kyotorphin, EPO, bFGF, hiralog, a lutenizing hormone releasing hormone (LHRH) analog, and neurotrophic factors chemical modification comprises the attachment of one or more polyethylene glycol residues to the bioactive peptide.

79. (original) The method of claim 56, wherein the fusion protein is further chemically modified.

80. (original) The method of claim 79, wherein the chemical modification comprises the attachment of one or more polyethylene glycol residues to the fusion protein.